



Sandhoff disease

Sandhoff disease is a rare inherited disorder that progressively destroys nerve cells (neurons) in the brain and spinal cord.

The most common and severe form of Sandhoff disease becomes apparent in infancy. Infants with this disorder typically appear normal until the age of 3 to 6 months, when their development slows and muscles used for movement weaken. Affected infants lose motor skills such as turning over, sitting, and crawling. They also develop an exaggerated startle reaction to loud noises. As the disease progresses, children with Sandhoff disease experience seizures, vision and hearing loss, intellectual disability, and paralysis. An eye abnormality called a cherry-red spot, which can be identified with an eye examination, is characteristic of this disorder. Some affected children also have enlarged organs (organomegaly) or bone abnormalities. Children with the severe infantile form of Sandhoff disease usually live only into early childhood.

Other forms of Sandhoff disease are very rare. Signs and symptoms can begin in childhood, adolescence, or adulthood and are usually milder than those seen with the infantile form. Characteristic features include muscle weakness, loss of muscle coordination (ataxia) and other problems with movement, speech problems, and mental illness. These signs and symptoms vary widely among people with late-onset forms of Sandhoff disease.

Frequency

Sandhoff disease is a rare disorder; its frequency varies among populations. This condition appears to be more common in the Creole population of northern Argentina; the Metis Indians in Saskatchewan, Canada; and people from Lebanon.

Genetic Changes

Mutations in the *HEXB* gene cause Sandhoff disease. The *HEXB* gene provides instructions for making a protein that is part of two critical enzymes in the nervous system, beta-hexosaminidase A and beta-hexosaminidase B. These enzymes are located in lysosomes, which are structures in cells that break down toxic substances and act as recycling centers. Within lysosomes, these enzymes break down fatty substances, complex sugars, and molecules that are linked to sugars. In particular, beta-hexosaminidase A helps break down a fatty substance called GM2 ganglioside.

Mutations in the *HEXB* gene disrupt the activity of beta-hexosaminidase A and beta-hexosaminidase B, which prevents these enzymes from breaking down GM2 ganglioside and other molecules. As a result, these compounds can accumulate to toxic levels, particularly in neurons of the brain and spinal cord. A buildup of GM2 ganglioside

leads to the progressive destruction of these neurons, which causes many of the signs and symptoms of Sandhoff disease.

Because Sandhoff disease impairs the function of lysosomal enzymes and involves the buildup of GM2 ganglioside, this condition is sometimes referred to as a lysosomal storage disorder or a GM2-gangliosidosis.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Beta-hexosaminidase-beta-subunit deficiency
- GM2 gangliosidosis, type 2
- GM2 Gangliosidosis, Type II
- Hexosaminidase A and B Deficiency Disease
- Sandhoff-Jatzkewitz-Pilz disease
- Total hexosaminidase deficiency

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Sandhoff disease
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0036161/>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Health Topic: Degenerative Nerve Diseases
<https://medlineplus.gov/degenerativenervediseases.html>
- Health Topic: Tay-Sachs Disease
<https://medlineplus.gov/taysachsdisease.html>

Genetic and Rare Diseases Information Center

- Sandhoff disease
<https://rarediseases.info.nih.gov/diseases/7604/sandhoff-disease>

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Lipid Storage Diseases Fact Sheet
<https://www.ninds.nih.gov/Disorders/All-Disorders/Lipid-storage-diseases-Information-Page>
- National Institute of Neurological Disorders and Stroke: Sandhoff Disease Information Page
<https://www.ninds.nih.gov/Disorders/All-Disorders/Sandhoff-Disease-Information-Page>

Educational Resources

- Disease InfoSearch: Sandhoff disease
<http://www.diseaseinfosearch.org/Sandhoff+disease/6408>
- MalaCards: sandhoff disease, infantile, juvenile, and adult forms
http://www.malacards.org/card/sandhoff_disease_infantile_juvenile_and_adult_forms
- March of Dimes
<http://www.marchofdimes.org/baby/tay-sachs-and-sandhoff-diseases.aspx>
- My46 Trait Profile
<https://www.my46.org/trait-document?trait=Sandhoff%20disease&type=profile>
- Orphanet: Sandhoff disease
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=796

Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases (CLIMB) (UK)
<http://www.climb.org.uk/>
- National Organization for Rare Disorders (NORD)
<https://rarediseases.org/rare-diseases/sandhoff-disease/>
- National Tay-Sachs and Allied Diseases Association
<https://www.ntsad.org/>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22Sandhoff+disease%22+OR+%22Gangliosidoses+GM2%22>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28Sandhoff+Disease%5BMAJR%5D%29+AND+%28Sandhoff+disease%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- SANDHOFF DISEASE
<http://omim.org/entry/268800>

Sources for This Summary

- Hendriksz CJ, Corry PC, Wraith JE, Besley GT, Cooper A, Ferrie CD. Juvenile Sandhoff disease--nine new cases and a review of the literature. *J Inherit Metab Dis.* 2004;27(2):241-9. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15159655>
- Tay SK, Low PS, Ong HT, Loke KY. Sandhoff disease--a case report of 3 siblings and a review of potential therapies. *Ann Acad Med Singapore.* 2000 Jul;29(4):514-7. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/11056783>
- Yoshizawa T, Kohno Y, Nissato S, Shoji S. Compound heterozygosity with two novel mutations in the HEXB gene produces adult Sandhoff disease presenting as a motor neuron disease phenotype. *J Neurol Sci.* 2002 Mar 30;195(2):129-38.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/11897243>

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